Case Report

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A Case Report of Metformin Related Lactic Acidosis

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Abstract

Metformin is an oral antidiabetic drug of the biguanide classused in type 2 diabetic patients with normal renal function. The mortality rate is high in cases of lactic acidos is developing in metformin intoxication. In the emergency department, metformin intoxication should be considered in the differential diagnosis of patients whouse metformin and have high anion gap metabolic acidosis (lactic acidosis). The most important and effective treatment with early diagnosis is correction of metabolic acidosis with hemodialysis or hemofiltration methods, bicarbonate treatment, adjustment of blood glucose level. Cardiovascular system support therapy significantly reduces morbidity/mortality. In this case report, we present the early diagnosis and successful treatment of a patient with lactic acidosis due to metformin intoxication.

Keywords: Metformin, Poisoning, Lactic Acidosis

Introduction

Poisoning; It is the situation that stops vital functions where a substance enters the living organism through mouth, skin, respiration, circulation, and damages its function (1). According to the first report of Turkish National Poison Control Center on the application by poisoning in Turkey is located medical drugs (69.74%) (1). Metformin is a biguanide group insulin-sensitizing drug used in the treatment of type 2 Diabetes Mellitus (DM) (2). Metformin exertsits effect by decreasing hepatic glucose production and gastrointestinal glucose absorption and increasing peripheral glucose utilization (2, 3, 4). The blood glucose lowering effect of metformin is largely due to the 25-30% decrease in endogenous glucose production. To a less erextent, it also decreases plasma glucose levels by increasing glucose uptake by skeletal muscles and adipose tissue. Unlike sulfonylurea group oral antidiabetics, it does not stimulate insulin release. It is excreted from the body through the kidney and may accumulate in the body due to decreased clearance in cases of renal failure (2, 3, 4, 5, 6). Side effects of metformin usually include gastrointestinal complaints such as nausea, anorexia, diarrhea, abdominal cramps and hypothermia (2, 4, 6). Side effects occur in more than 50% of patients. The most important known side effect of metformin is lactic acidosis, which has a high mortality rate and should not be used in patients with creatinine levels>1.4 mg/dL (2, 3). Metformin-induced lactic acidosis is characterized by high blood lactate concentration, decreased blood pH and electrolyte disorders with increased anion gap. Although lactic acidosis due to metformin use has a beter prognosis than other types of lactic acidosis, reported mortality rates can be as high as 25-50%. According to current guidelines, if the estimated glomerular filtration rate (eGFR) falls to<45 mL/min/1.73 m2, the dose of metformin should be reviewed. In patients with an estimated GFR <30 mL/min/1.73 m2, drug use should be stopped. The oretically, impaired renal function decreases GFR and this increases metformin accumulation in the body (2, 3, 4). In this case, a patient hospitalized in the internal medicine clinic because of lactic acidosis due to metformin intoxication was successfully treated with early diagnosis.

Case Report

A 57 years old woman was admitted to the emergency department with vomiting, confusion and low blood glucose. According to the anamnesis obtained from the patient, she had consulted to the family physician with the same complaints about 1 hour ago and the patient's blood glucose level was 55 mg/dl at the family health center, dextrose infusion was started and the patient was referred to the emergency department when her complaints persisted although her blood glucose level increased to around 200 mg/dl. It was learned that the patient had diabetes mellitus and was taking metformin for this reason. When the drugs used by the patient were questioned, he stated that he used metformin irregularly. For this reason, he

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stated that he had taken extra metformin tablets recently. Initial evaluation of the patient was performed in the emergency department. Blood tests of the patient were analyzed. Blood glucose, sodium, calcium and carbonmonoxide values were found to be with in the normal range. Creatinine value was 0.94 mg/dL (minimally elevated). Computerized brain tomography and diffusion MRI performed due to clouding of consciousness revealed no pathology. In the venous blood gas analysis of the patient; pH: 7.2, pCO_2: 35.4 mmHg, pO_2: 40.4 mmHg, lactate: 13.5 mmol/L, metabolic acidosis with anion gap and increased base deficit was present. A differential diagnosis was made to explain vomiting, confusion and lactic acidosis and metformin-associated lactic acidosis was considered. The patient was hospitalized in the internal medicine clinic. In the continuation of the treatment, the general condition of the patient improved and the blood gas obtained during the treatment process showed pH: 7.29, pCO_2: 41 mmHg, lactate: 9.5mmol/L. Base deficit and bicarbonate were with in normal range. In the arterial blood gas analysis of the patient in the 1st week of treatment; pH: 7.38, pCO_2: 43 mmHg, pO_2: 97 mmHg, HCO_3: 24.3mmol/L and lactate: 1.2 mmol/L, his general condition improved completely and he was discharged with recovery.

Discussion

Metformin is a drug from the biguanide groupu sed in the treatment of type 2 diabetes mellitus (2). In high dose metformin intake, nonspecific symptoms including anorexia, lethargy, nausea, vomiting and epigastric pain as well as life-threatening symptoms including moderate renal failure, hypotension, hypothermia, respiratory failure and cardiac rhythm disturbances may develop (2, 3, 4, 7). Our patient had nausea/vomiting, minimally elevated creatinine levels and confusion. Eosinophilia in peripheral blood, hematuria and proteinuria in urine are possible findings in cases of interstitial nephritis (2, 3, 4). In our case, eosinophilia and hematuria/proteinuria in urine analysis were absent.

Lactate is one of the end products of anaerobic glycolysis. Lactate is utilized by hepatocytes and converted to glucose through gluconeogenesis. Normal blood lactate levels range between 0.5 and 1 mmol/L. Blood lactate levels greater than 2 mmol/L are defined as hyperlactatemia. Lactic acidemia occurs when serum lactate concentration exceeds 4 mmol/L with pH less than 7.35. In general, elevated lactate levels result from increased production or decreased urinary excretion. Etiology of the anaerobic metabolism required to cause a lactic acidosis includes various disease processes such as sepsis, hemorrhagic shock, cardiac arrest, trauma, intoxications (such as: metformin poisoning, metabolic poisons such as cyanide), burns, diabetic ketoacidosis, cancers and intense muscle activity (8). In a study by Wills et al. the incidence of metformin-induced severe lactic acidosis was reported to be 9.1% in patients who received a single over dose of metformin (9). In another study conducted by Li Cavoli et al. among 1014 renal patients, it was reported that acute renal failure accompanied by lactic acidosis was detected in 47 patients who used metformin for hyperglycemia control (10). In another case of metformin intoxication reported by Mustafa et al., acute renal failure with lactic acidosis and hypothermia was reported (11). In our case, there was an elevated lactate level in the blood gas obtained at the first presentation. In articles in the literature reporting the development of metformin-induced lactic acidosis and acute renal failure, it has been reported that hemodialysis is usually performed in treatment (12). In our patient, blood creatinine levels were found to be minimally elevated and normalized with hydration/fluid support. Hemodialysis was not performed. The effects of metformin on the kidney are thought to be related to renal hypoperfusion or direct renal toxic effect of metformin (12).

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